ment that "this effect was independent of foreign travel" does not appear to be justified. Indeed, Nelson et al.'s report of a significantly ($P = .01$) decreased mean duration of hospitalization associated with ciprofloxacin-resistant *Campylobacter* infection (compared with ciprofloxacin-susceptible *Campylobacter* infection) is inconsistent with the conclusion that adverse consequences to human health derive from resistant infections.

Finally, the recommendation "Additional efforts are needed to preserve the efficacy of fluoroquinolones" (p. 1150) does not follow from either the data or the analyses that Nelson et al. present; their data do not demonstrate a significantly increased duration of diarrhea in patients infected with *Campylobacter* strains that can be classified as fluoroquinolone resistant ($P = .2$), nor do they address the matter of ciprofloxacin's efficacy against resistant strains of *Campylobacter*. Their data show that, compared with cases of *Campylobacter* infection acquired domestically, cases acquired during foreign travel have both a greater likelihood of resistance to fluoroquinolone *and* more days of diarrhea; but this should not be confused with the assertion (implicit in Nelson et al.'s title) that excess days of diarrhea are *caused by* (or "Due to") resistance to ciprofloxacin, rather than by other foreign travel–related factors.

Louis Anthony Cox, Jr.,[1,2] Dennis Copeland,[3] and Michael Vaughn[3]

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Potential conflicts of interest: L.A.C. has been a paid consultant for the US Food and Drug Administration's Center for Veterinary Medicine, the Animal Health Institute, and Bayer HealthCare, with regard to the potential risk that the use of fluoroquinolones in poultry poses to human health. D.C. and M.V. are employed by Bayer, the manufacturers of Baytril (enrofloxacin), a fluoroquinolone approved for use in poultry.

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Reply to Cox et al.

To the Editor—Repeating comments they had made previously [1, 2], Cox et al. [3] have provided a critique of our analysis of the FoodNet *Campylobacter* case-control study. Data from the FoodNet study, the largest reported case-comparison study of clinical outcomes of *Campylobacter* infections, demonstrated that resistance to fluoroquinolone (e.g., ciprofloxacin) is common in *Campylobacter* infections in humans and that persons with ciprofloxacin-resistant *Campylobacter* infection have a longer duration of diarrhea than do persons with ciprofloxacin-susceptible *Campylobacter* infection. Using standard epidemiologic principles, we found a consistent, strong, and robust association between having a longer mean duration of diarrhea and ciprofloxacin-resistant *Campylobacter* infection [4].

When Cox et al. examined the FoodNet data, which were obtained under the Freedom of Information Act, they concluded that foreign travel confounded the association between resistance to ciprofloxacin and duration of diarrhea. Their analysis, which did not consider the effect of taking antidiarrheal medication, concluded that resistance to ciprofloxacin was not associated with an increased duration of diarrhea. In the analysis conducted by the Centers for Disease Control and Prevention, state health departments, the US Department of Agriculture, and the US Food and Drug Administration (FDA), we included foreign travel as a variable in the analysis and found that, when antidiarrheal medication is included in the model, the inclusion of foreign travel does not change the observed consistent association between resistance to ciprofloxacin and duration of diarrhea; foreign travel is not consistently or strongly associated with a longer duration of diarrhea, nor does it confound the observation that resistance to ciprofloxacin is associated with a longer duration of illness. As we noted in our article [4], taking antidiarrheal medication is associated with duration of diarrhea; failure to include the effect of antidiarrheal treatment leaves a major associated factor uncontrolled, producing spurious results.

We do not agree with the supposition by Cox et al. that ciprofloxacin-resistant *Campylobacter* infections are less common now than they were during 1998. The incidence of laboratory-confirmed *Campylobacter* infection has declined in the United States in recent years, as indicated by FoodNet surveillance data [5], but the prevalence of *Campylobacter* resistance to ciprofloxacin has increased [6, 7]. When both the decline in the incidence of laboratory-confirmed *Campylobacter* infection and the increase in the prevalence of *Campylobacter* resistance to ciprofloxacin are taken into account, the incidence of ciprofloxacin-resistant *Campylobacter*

infection increases an estimated 46%, from 1.4 infections/100,000 persons during 1997 to 2.0 infections/100,000 persons during 2001 [8].

Readers interested in the legal context of this discussion, including the administrative law judge's initial decision to uphold the FDA's proposed prohibition of the use of fluoroquinolones in poultry, are referred to FDA docket number 00N-1571 [9].

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Safety of Stavudine during Pregnancy

To the Editor—In the 15 December 2004 issue of the *Journal of Infectious Diseases*, Wade et al. present a study that is inappropriately entitled "Pharmacokinetics and Safety of Stavudine in HIV-Infected Pregnant Women and Their Infants: Pediatric AIDS Clinical Trials Group Protocol 332" [1]. The pharmacokinetic work is necessary and commendable, but it is impossible to assess, even grossly, the tolerance to this molecule after perinatal exposure with such a small number of study participants ($n = 10$). It is not reasonable to include the notion of safety in the title and to conclude in the Abstract and Discussion that this molecule is safe to use during pregnancy.

In addition, Wade et al. raised no questions concerning the potential interference of nucleoside analogues with mitochondrial [2–7] or nuclear [8] DNA in the fetus. Regardless of how we choose to interpret the increasing quantity of data from studies in animals and humans on this type of toxicity, these data cannot be ignored. I understand that it was not the aim of Wade et al.'s study to identify specific biological markers, but it is interesting to note that hypoglycemia ($n = 1$) and hyperkalemia ($n = 3$) may be such indicators.

Furthermore, the limited hematologic data presented by Wade et al. should not be underemphasized: 5 of the 10 infants in their study developed grade 3 neutropenia, which does not correspond with what has been observed after exposure to zidovudine [9] or the combination of zidovudine and lamivudine [10].

The issue of tolerance to nucleoside analogues after perinatal exposure is important. It deserves more than the type of superficial analysis presented by Wade et al., which may give hurried readers the impression that these molecules can be used safely during pregnancy. For most antiretroviral molecules, this has not yet been established by means of appropriate studies, both in terms of numbers of participants and appropriate biological markers.

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